Epidemiologic study on "Yusho", a poisoning caused by rice oil contaminated with polychlorinated biphenyls

by

Masanori Kuratsune, Takesumi Yoshimura,
Junichi Matsuzake, and Atsuko Yamaguchi

Department of Public Health, Faculty of Medicine,
Kyushu University

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Sporadic outbreaks of a peculiar skin disease which was later called as "Yusho" were first reported in Fukuoka-Ken (Fukuoka prefecture), Japan, in early October 1968. It was characterized by such symptoms as follicular accentuation, acneform erruption, pigmentation of the skin and nails, hypersecretion of the Meibomian gland, increased sweating at palms, feeling of weakness, and numbness in limbs. The epidemic spread not only over Fukuoka-Ken but also over 20 other prefectures in the western part of Japan, producing about 1,000 patients. In order to clarify the cause of the epidemic we conducted an epidemiologic investigation of 325 patients seen in Fukuoka-Ken from October 1968 until January 1969, under a close cooperation with the health departments.

1. Descriptive epidemiologic study

Ninety-nine percent of the patients were affected during 1968 and 55 percent of the cases were concentrated from June to August. The geographical distribution of the patients as observed by calculating crude incidence rates did not indicate any common socioeconomic or environmental factor which might be connected with the disease. A distinct familial aggregation was noted because the 325 patients belonged to 112 families. Both sexes, irrespective of age, were shown to be equally affected.

2. Analytical epidemiologic studies.

When our study started, a brand of rice oil produced by

K company (abbreviated as K rice oil) had vaguely been suspected as a possible cause of the disease. Therefore, a thorough investigation was undertaken to determine whether the patients with Yusho had actually used such brand of oil before affected. It was soon disclosed that all the patients had used K rice oil, either canned or bottled. Furthermore, an astonishing fact was shown that, no matter where they lived, 166 of the 170 patients who used the canned oil had used a very specific oil produced or shipped by the K company on February 5 and 6, 1968 and 143 of the 155 patients who used the bottled oil exclusively might have bought the oil shipped from the company in the period February 6 to 15, 1968. Thus, nearly all of the patients had had a very peculiar common experience of use or possible use of a rice oil produced or shipped by one company in a specific period. The attack rate was as high as 63.9 percent for those who consumed the specific canned oil.

In an additonal survey, we could demonstrate that a group of 113 persons who regularly used K rice oil but did not use the specific K rice oil produced or shipped in the period in question were free of the disease.

In order to know whether any other factors than the rice oil might be the cause of the epidemic, we also made two case-control studies by home interviews. In one, the personal backgrounds of the patients and of their matched controls were compared, while in the other, the use of oils and fats in the patient households and in the control households were compared.

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In the former comparison, only one of 60 personal factors examined, namely habit of "eating fried foods or tempura nearly every day", was significantly more commonly seen among the patients than among the controls. In the latter investigation, a distinct and significant difference was noted between the two groups only for use of rice bran oil. About 96 percent of the patients households had used rice bran oil regularly while only 31 percent of the control households had. When asked about the use of K rice oil, all of the patients households affirmed it. Thus, the case-control studies clearly indicated that none of the factors tested except use of K rice oil could account for the disease.

3. Dose-response relationship

A rough estimation of the quantity of the specific K rice oil consumed by each patient and his family members was made disregarding their age, sex, food intake, and possible loss of oil during and after cooking. A definite dose-response relationship was noted in attack rate as well as in clinical severity.

Thus, all the above epidemiologic findings proved that ingestion of the K rice oil produced or shipped in the specific period of time is the cause of the epidemic.

4. Toxic agent

The chemical study group of the disease (Chief: Prof. H. Tsukamoto, Kyushu University) discovered that the canned K

rice oil produced or shipped on February 5, 1968 and used by some of the patients had been contaminated with about 2,000 ppm of Kanechlor 400, a brand of polychlorinated biphenyls, which is considered to have leaked from the heating pipe of the oil in the process of production. Skin fat collected from the patients also contained Kanechlor. Gaschromatographic analysis of 109 samples of the bottled K rice oil proved that a significant contamination of the bottled oil was limited only to those shipped between February 7 to 10, 1968. Thus, the results of chemical analysis perfectly coincided with those of epidemiologic approaches.

The minimum total dose of Kanechlor 400 to cause the disease was estimated to be around 0.5 g.

5. Other observations

Thirteen women consisting of 10 with Yusho and two unaffected and one status-unspecified wives of patients were shown to have delivered 10 live born and two stillborn infants during the specified period. These infants and fetuses had grayish darkbrown stained skin, nail, and gingiva, and an increased eye-discharge at birth. As they grew older, their stained skin gradually faded. The majority of the babies were small for their periods of gestation.

The affected school children were compared with matched unaffected children for growth. The gains of the affected boys in height and weight was shown to have decreased after the

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poisoning, while the affected girls showed no definite change in this respect.

Many patients with Yusho are still tortured by the disease even after more than 3 years. To cure them and to prevent another epidemic of Yusho, all possible world-wide cooperative efforts are highly desired.